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Positive Margins of Breast Biopsy: Is Reexcision Always Necessary?

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Background and Objectives: Breast-conserving surgery requires excision of all gross tumor and subsequent radiation therapy. It is generally accepted that the presence of microscopically positive margins requires reexcision. The goal of this study was to identify characteristics that distinguish breast biopsy specimens with positive margins that when reexcised are free from residual tumor. This population of patients may benefit from breast irradiation only, without the need for another surgical procedure.

Methods: One hundred and fifteen of 395 cancer-proven biopsies had positive surgical margins and were treated with reexcision or mastectomy. Sixty-seven of these were negative for residual tumor and 48 were positive for residual tumor. Evaluation for tumor type, tumor size, grade, presence of vascular invasion, volume of the biopsy specimen, true positivity and the number of positive margins, multifocality of the tumor, and type of anesthesia was done by univariate and multivariate analysis.

Results: Univariate and multivariate analysis revealed that factors associated with a positive reexcision included margin status, method of detection, histologic appearance, and type of anesthesia used.

Conclusion: These results suggest that small, clinically detectable unifocal tumors could be treated without the need for a further excision. Eradication of microscopic residual tumor could be done by irradiation only, sparing the patient an additional surgical procedure.

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KEY WORDS: **breast biopsy; breast neoplasms; specimen margins; reexcision**

INTRODUCTION

The advent of breast-conserving surgery in appropriate breast tumors has allowed an adequate therapeutic advantage while at the same time ensuring a better cosmetic result along with a shorter hospital stay. Ideally, breast-conserving surgery requires excision of all gross tumor and subsequent radiation therapy to ensure sufficient local control [1,2]. However, the extent of surgical resection beyond gross excision, and specifically the importance of microscopically negative margins, remains unclear [3–5]. It is generally accepted that the presence of microscopically positive margins requires reexcision [4]. This reexcision is considered important to ensure the eradication of tumor tissue from the breast in order to decrease the risk of local recurrence. Interestingly, a sizable percentage of reexcisions results in a specimen free of residual tumor. Thus, in retrospect, these reexcisions may not contribute to disease control, but do add associated morbidity, cost, and possible compromise of an

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acceptable cosmetic result. It would be desirable to be able to predict in which case a reexcision will most probably be negative or positive, and then to proceed with reexcision only in those cases that most likely would benefit from it.

The goal of our study was to determine whether we could identify characteristics that distinguish breast biopsy specimens with positive microscopic margins that, when reexcised, are free of residual tumor. This would allow us to identify a population of patients whom it may be feasible to treat with breast irradiation only without the need for another surgical procedure.

MATERIALS AND METHODS

Between 1991 and 1995, 2,017 breast biopsies were performed at the Department of Surgical Oncology, Chaim Sheba Medical Center, Tel Hashomer, Israel. The primary excisional procedure was designed to excise completely the tumor with a margin of at least 1–2 cm of grossly normal breast tissue. No frozen sections were done on the specimens. All excisional biopsy specimens were marked with orienting sutures and the surface was painted with Indian ink. Margins were defined as positive when cancer was present at the surgical margin (true positive) or when cancer was present less than 2 mm from the inked edge (close positive). During this time period, 395 biopsies (19.6%) were positive for cancer. One hundred and fifteen (29%) of them had positive surgical margins and were treated with reexcision or mastectomy.

All primary biopsy specimens were examined and evaluated for tumor type, tumor size, grade, presence of vascular invasion, volume of the biopsy specimen, true positivity and number of positive margins, and whether the tumor was multifocal. Reexcision was accomplished by reexcising the previous biopsy cavity with a margin of 1–2 cm normal breast tissue or by mastectomy. The specimen that was reexcised was evaluated for presence of residual tumor, microscopic or macroscopic involvement, and whether the pathology was similar to the primary tumor. Other factors examined were the use of fine-needle localization for the primary excision, the use of local or general anesthesia for the primary excision, and the presence of positive lymph nodes in patients undergoing axillary dissection. Univariate analysis was performed to determine predictive information from each variable independently, and this was followed by multivariate analysis to assess the most significant prognostic factors.

Statistical Method

Differences in patient characteristics between the positive and negative reexcision groups were assessed by the Chi-square test for categorical variables and analysis of variance for continuous variables. *P* values are based on two-tailed tests; $P < 0.05$ was considered statistically significant. A forward stepwise multivariate logistic regression model was applied to determine potential risk factors for reexcision while controlling for confounding variables. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated.

RESULTS

Of the 2,017 breast biopsies performed at our institution, 395 (19.6%) were positive for cancer. The average age of the cancer patients was 56.1 ± 13. One hundred and fifteen (29%) of these cancer-proven biopsies had positive surgical margins and were treated with reexcision (75) or mastectomy (40). Of the 115 reoperations, 67 (58%) were negative for residual tumor. Forty-eight (42%) of the reoperations were positive for residual tumor, but in half there was only microscopic residual disease. The group of negative reexcisions included 12 (18%) mastectomies.

Univariate analysis (Table I) revealed that the factors that significantly correlated with positive reexcisions were method of detection ($P = 0.0001$), the use of fine-needle localization ($P = 0.007$), the type of anesthesia used for the biopsy ($P = 0.004$), the size of the specimen ($P = 0.0001$), the size of the tumor ($P = 0.0001$), multifocal disease ($P = 0.0001$), presence of vascular invasion ($P = 0.002$), pathologic grading ($P = 0.0001$), true vs. close positive margins ($P = 0.0001$), number of involved margins ($P = 0.0001$), and presence of disease in the axillary nodes ($P = 0.0001$). The average specimen volume for negative reexcisions was 53.3 ± 32.1 cc^3, which was significantly larger than that for positive reexcisions (32.8 ± 17.8 cc^3; $P = 0.0001$). Patients with smaller tumors or those with invasive ductal carcinoma without an intraductal component and those with a lower pathological grade were less likely to have a positive reexcision. In our series, 47% of reexcision specimens of true positive excisional biopsies were positive for residual tumor compared with only 7% of the close positive. When more margins were involved, it significantly increased the rate of positive reexcision ($P = 0.0001$), as did the presence of involved regional lymph nodes ($P = 0.0001$). The results of the multivariate analysis are summarized in Table II. In multivariate analysis, adjusting for all the factors that were significant in univariate analysis, the most significant risk factor for positive reexcision was the number of true margins involved (odds ratio = 35.8 for two positive margins and 59.4 for more than two margins vs. one margin, $P = 0.02$).

Multifocality, nonpalpable mammographically detected lesion, and the use of local anesthetics for the biopsy procedure were of borderline significance in the multivariate model. The large confidence intervals for all the variables in Table II are due to moderate sample size and high correlations between some coefficients (corre-

TABLE I. Factors Affecting a Positive Reexcision After a Breast Biopsy With Positive Margins

	Negative reexcision (n = 67)	Positive reexcision (n = 48)	*P*
Age (mean ± SD)	58.1 ± 13.4	54.1 ± 11.1	0.09
Clinical or mammographic findings			
Palpable	29 (43.3%)	6 (12.5%)	0.0001
Mammographic architectoral change	5 (7.5%)	2 (4.2%)	
Mass	24 (35.8%)	8 (16.7%)	
Microcalcifications	9 (13.4%)	32 (66.7%)	
Fine-needle localization	32 (47.8%)	35 (72.9%)	0.007
Type of anesthesia			
General	34 (50.8%)	14 (29.2%)	0.004
Local	33 (49.2%)	34 (70.8%)	
Specimen size, volume (mean ± SD)	53.1 ± 32.1cc^3	32.8 ± 17.8cc^3	0.0001
Tumor size (mean ± SD)	1.6 ± 1 cm	2.5 ± 0.9 cm	0.0001
Multifocal disease	5 (7.5%)	24 (50.0%)	0.0001
Vascular invasion	4 (6.0%)	13 (27.1%)	0.002
Pathology			
Infiltrating duct cancer (IDC)	30 (44.8%)	9 (18.8%)	0.07
Ductal carcinoma in situ (DCIS)	5 (7.5%)	4 (8.3%)	0.56
IDC + DCIS	29 (43.3%)	32 (66.7%)	0.02
LCIS	3 (4.5%)	3 (6.2%)	
Pathological grade			
1	25 (37.3%)	1 (2.1%)	
2	29 (43.3%)	28 (58.3%)	0.0001 (1 vs. 2+)
3	9 (13.4%)	15 (31.2%)	
N/A	4 (6.0%)	4 (8.3%)	
Positivity of margins			
True	15 (22.4%)	34 (70.8%)	0.0001
Close	51 (76.1%)	12 (25.0%)	
N/A	1 (1.5%)	2 (4.2%)	
Number of margins involved			
1	55 (82.1%)	6 (12.5%)	
2	8 (11.9%)	18 (37.5%)	
3	2 (3.0%)	23 (47.9%)	0.0001
4	1 (1.5%)	1 (2.1%)	
N/A	1 (1.5%)		
Positive lymph nodes	12 (17.9%)	28 (58.3%)	0.0001

TABLE II. Risk Factors for Positive Findings for Cancer in Reexcision Breast Biopsy*

Risk factor	OR	95% CI	*P*
Number of true margins involved (>2 vs. 1)	43.7	8.1–237	0.02
Mammographically detected vs. palpable	24.3	2.4–244	0.08
Local anesthesia vs. general	10.4	1.7–64	0.12
Multifocal disease	16.4	2.4–114	0.09

*Adjusted for age, grade, size, pathology, and fine-needle localization.

lation coefficient between number of margins and mode of anesthesia = 0.50).

DISCUSSION

Breast-conservation surgery and radiation therapy produce survival rates comparable to modified radical mastectomy [1,2]. However, the optimal extent of local tumor excision required prior to irradiation has not been established. Although leaving gross residual tumor has a profound impact on recurrence, much less is known about the necessity to obtain microscopically negative margins. The opinions in the literature are split about the contribution of microscopically positive margins to local failure [3–7]. However, current recommendations include appropriate attention to surgical margins, including circumferential specimen inking, orientation, and proper pathologic examination [8].

Nevertheless, a significant number of patients with properly analyzed biopsy specimens found to have positive margins have no residual tumor on reexcision. We had a 58% negative reexcision rate, including 12 mastectomies. The frequency of residual tumor in relumpectomy specimens ranges from 32% to 63%, and in about half of the specimens only a minimal amount of microscopic disease was found [4,9–13].

In view of the uncertainty of the impact of microscopically involved margins on local recurrence and survival, the above information suggests that some reoperations

TABLE III. Possible Predicting Factors for Positive Cancer Finding in Reexcision Breast Biopsies: Review of Literature

	Jardines et al. [13][a]	Gwin et al. [8]	Acosta et al. [15]	Schnitt et al. [9]	Anscher et al.[a] [7]	Kearney et al. [16]	Schmidt-Ullrich et al. [3]	Present series[a]
1. Mammographically detected finding	+							+
2. Tumor size/stage	+	+	+			+	+	
3. Histologic appearance	+							
4. Extensive intraductal component				+	+			
5. Involvement of axillary lymph nodes	+							
6. Margin status of primary excision		+			+	+		+
7. Type of anesthesia								+
8. Multifocal disease								+

[a]Multivariate analysis.

might not be justified. If one considers the cosmetic compromise of reexcisions and the fact that sometimes a mastectomy is carried out in order to achieve clean margins, this surgical procedure may unnecessarily damage the patient. It would therefore be helpful to identify clinical and pathological criteria that could help in determining when a reexcision is unnecessary.

The definition of positive margins in the literature is unclear. According to some authors only macroscopically or microscopically involved margins should be defined as positive, whereas others define it as involvement of the breast 2 mm or less from the resected surface [2]. Positivity is regarded by Ryoo et al. [5] as involvement of 5 mm or less from the inked edge. We defined as true positive the presence of cancer either macro- or microscopically at the inked margins and involvement of 2 mm or less from the cut surface as close positive.

In the present series, multivariate analysis of the factors found to correlate with a positive reexcision included the number of true margins involved with the disease and the presence of multifocal disease. The mode of detection (mammography vs. physical examination) and the type of anesthesia used for the primary excisional biopsy (local vs. general) were also predictors for positive reexcisions with residual tumor.

In a previous work [14], we have shown that the type of anesthesia affects the rate of positive margins found at pathological examination of the biopsy specimen. The type of anesthesia also correlated with the size of specimen excised. One should remember that the amount of breast tissue removed adversely affects the cosmetic results. However, cosmetics should not be achieved at the expense of a higher local recurrence rate.

Finding residual disease at the time of reexcision has been reported to correlate with the size of the primary tumor, the status of the initial resection margin, method of detection, presence of microcalcifications, performing a limited biopsy, the pathologic status of the axillary lymph nodes, and the presence of extensive intraductal component [13]. Over the past several years, a number of groups examined possible predictive factors for positive reexcision [3,7–9,13,15,16], although only two used multivariate analysis [7,13]. These studies and the present series are summarized in Table III. The tumor size and the true margin status of the primary excision were the most commonly noted factors.

These results and our present survey suggest that small, clinically detectable unifocal tumors with close positive margins could probably be treated without the need for a further excision. Further eradication of possible microscopic residual tumor could be done by radiation treatment alone, thus sparing the patient an additional surgical procedure.

A close cooperation between the surgeon and the pathologist would be helpful to minimize the rate of margin positivity. Macroscopic and frozen section examination of the resected specimen as well as the use of the touch-prep technique of the surgical margins may reduce the rate of involved margins. The use of other modalities, such as intraoperative sonography and radio-labeled antibodies with a gamma detecting probe, may also increase the number of complete excisional biopsies.

In summary, a few factors correlating with a positive reexcision were found: tumor size, method of detection, the histologic appearance, the number of the involved margins, the presence of extensive intraductal component, multifocality, nodal status, and the type of anesthesia used for the primary excision. Those patients with clinically detected, relatively small unifocal infiltrating cancers with close positive margins could possibly be treated without reexcision with breast radiation and a boost to the excisional field.

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